Claims

What is claimed is:

1. A device for characterizing the binding forces between a first binding member and a second binding member, the device comprising

a surface that has a first binding member attached thereto,

one or more particles that have a second binding member attached thereto,

a reaction vessel that includes means for exposing the surface to the particles whereby, if the first binding member has a binding affinity for the second binding member, a complex is formed between individual first binding members and individual second binding members and the particles thereby become immobilized with respect to the surface,

ultrasonic force means operatively disposed with respect to the surface for applying a variable force on the particles, and

means for monitoring the position of the particles with respect to the surface.

2. The device of Claim 1 wherein the variable force on the particles can be varied between an amount of force that is insufficient to separate the complex between the first binding member and the second binding member and an amount of force that is sufficient to separate the complex.

3. The device of Claim 1 wherein the ultrasonic force means is an ultrasonic transducer capable of applying a pulsed ultrasonic force, and wherein the amplitude, frequency, pulse duration

and/or wave-form of the ultrasonic force are selectable.

4. The device of Claim 3 wherein the frequency of the pulsed ultrasonic force is between about 80 kHz and about 10 MHz.

5. The device of Claim 1 wherein the pulse duration of the pulsed ultrasonic force is less than about 20 milliseconds.

6. The device of Claim 1 wherein the wave-form of the pulsed ultrasonic force is a triangle or saw-tooth.

7. The device of Claim 1, wherein said means for monitoring the position of the particles with respect to the surface comprises an optical microscope.

8. The device of Claim 7, wherein said position-monitoring means further comprises a digital image acquisition system.

9. The assay device of Claim 8, wherein said position monitoring means further comprises a digital image processing system, for identifying images of particles.

10. The device of Claim 1, further comprising a counting means for counting particles.

11. The device of Claim 1, wherein said particles have an average diameter between about 5 nm and about 1 mm.

12. The device of Claim 1 wherein the particles are magnetic and wherein the device further includes means for applying a magnetic force to the particles.

13. The device of Claim 1 wherein the device further includes means for applying additional force to the particles, said additional force being selected from the group consisting of magnetic

force, optical force, hydrodynamic force, electrostatic force, gravitational force and combinations thereof.

14. A device for characterizing the binding forces between a plurality of different surface-bound binding members and a particle-bound binding member, the device comprising

a surface that has spatially distinguishable subregions, wherein each subregion has a different surface-bound binding member attached thereto,

a plurality of particles that have a particle-bound binding member attached thereto,

a reaction vessel that includes means for exposing the subregions of the surface to the particles whereby, if a surface-bound binding member has a binding affinity for a particle-bound binding member, a complex is formed between individual surface-bound binding members and individual particle-bound binding members and the particles thereby become immobilized with respect to the surface,

ultrasonic force means operatively disposed with respect to the surface for applying a variable force on the particles, and

means for monitoring the position of the particles with respect to the subregions of the surface.

15. A device for characterizing the binding forces between a surface-bound binding member and a plurality of different particle-bound binding members, the device comprising

a surface that has a surface-bound binding member attached thereto,

a plurality of particles of different distinguishable classifications wherein each different

distinguishable classification of particles has a different particle-bound binding member attached thereto,

a reaction vessel that includes means for exposing the surface to the particles whereby, if a surface-bound binding member has a binding affinity for a particle-bound binding member, a complex is formed between individual surface-bound binding members and individual particle-bound binding members and the particles thereby become immobilized with respect to the surface,

ultrasonic force means operatively disposed with respect to the surface for applying a variable force on the particles, and

means for distinguishing between particles of different classifications and for monitoring the position of particles of each classification with respect to the surface.

16. A device for characterizing the binding force between a first binding member and a second binding member, the device comprising

at least one assay cell that includes a cell wall having an outside surface and an inner surface surface, wherein the inner surface surface has been chemically modified by the attachment of a first binding member

a test medium including one or more particles that have been chemically modified by the attachment of a second binding member,

a reaction vessel that includes means for exposing the surface to the test medium whereby, if the first binding member has a binding affinity for the second binding member, a

complex is formed and the particles thereby becomes immobilized with respect to the surface,

ultrasonic force means in contact with the outer surface of the assay cell and operatively disposed with respect to the surface for applying a variable ultrasonic force through the cell wall and onto the inner surface, and

means for monitoring the position of the particles with respect to the surface.

17. An assay device for detecting the presence or amount of an analyte in a test sample, the assay device comprising

a surface that has binding members that bind specifically to an analyte attached thereto,

means for exposing the surface to the test sample,

a labeled reagent that, when exposed to a surface that has been exposed to the test sample, becomes immobilized with respect to the surface specifically in relation to the amount of the analyte in the test sample,

ultrasonic force means operatively disposed with respect to the surface for applying an ultrasonic force onto the surface for dislodging any of the labeled reagent that binds non-specifically to the surface or that becomes immobilized on the surface due to cross-reactivity with an analog of the analyte, and

means for detecting the amount of labeled reagent that is immobilized with respect to the surface.

18. The assay device of claim 17 wherein the ultrasonic force means is an ultrasonic transducer capable of applying a pulsed ultrasonic force, and wherein the amplitude, frequency, pulse

duration and/or wave-form of the ultrasonic force are selectable so that the ultrasonic force is sufficient to remove from the surface any of the labeled reagent that binds non-specifically to the surface or that cross-reacts with the an analog of the analyte, and so that the ultrasonic force is insufficient to remove any analyte that binds to the binding member and any labeled reagent that becomes immobilized on the surface in relation to the amount of analyte.

19. An assay device for detecting the presence or amount of an analyte in a test sample, the assay device comprising

a surface that has first binding members that bind specifically to an analyte attached thereto,

means for exposing the surface to the test sample,

a plurality of particles that have second binding members attached thereto, wherein the second binding members are capable of undergoing a selective binding interaction whereby the particles, when exposed to the surface that has been exposed to the test sample, become immobilized specifically with respect to the surface in relation to the amount of the analyte in the test sample,

ultrasonic force means operatively disposed with respect to the surface for applying an ultrasonic force onto the surface for dislodging any of the particles that bind non-specifically to the surface or that become immobilized on the surface due to cross-reactivity of the second binding member with an analog of the analyte, and

means for monitoring the position of the particles with respect to the surface.

20. The assay device of Claim 19, wherein the position-monitoring means comprises an optical microscope.

21. The assay device of Claim 20, wherein the position monitoring means further comprises a digital image acquisition system.

22. The assay device of Claim 21, wherein the position-monitoring means further comprises a digital image processing system, for identifying images of particles.

23. The assay device of Claim 19, further comprising a counting system adapted for counting particles.

24. The assay device of Claim 19, wherein the particles have an average diameter between about 5 nm and about 1 mm.

25. An assay device for simultaneously detecting the presence or amount of a plurality of different analytes in a test sample, the assay device comprising

a surface that has spatially distinguishable subregions, wherein each subregion has a different surface-bound binding members attached thereto, wherein each different surface-bound binding member binds specifically to a different analyte,

means for exposing the surface to the test sample,

a plurality of sets of particles that have particle-bound binding members attached thereto, wherein the particle-bound binding members are capable of undergoing a selective binding interaction whereby the particles, when exposed to the surface that has been exposed to the test sample, become immobilized specifically with respect to the surface in relation to the amount of

an analyte in the test sample, and wherein each set of particles is selective of a different analyte,

ultrasonic force means operatively disposed with respect to the surface for applying an ultrasonic force onto the surface for dislodging any of the particles that bind non-specifically to the surface or that become immobilized on the surface due to cross-reactivity of a particle-bound binding member with an analog of an analyte, and

means for monitoring the position of the particles with respect to the subregions of the surface.

26. An assay device for detecting the presence or amount of an analyte in a test sample, the assay device comprising

a plurality of first particles that have first binding members that bind specifically to an analyte attached thereto,

a reaction vessel that includes means for exposing the plurality of first particles to the test sample,

a plurality of second particles that have second binding members attached thereto, wherein the second binding members are capable of undergoing a selective binding interaction whereby the second particles, when exposed to first particles that have been exposed to the test sample, bind to the first particles in relation to the amount of the analyte in the test sample and form an aggregate,

ultrasonic force means operatively disposed for applying an ultrasonic force to the reaction vessel for dislodging any of the analyte or second particles that bind non-specifically to

the first particles or that bind to the first particles due to cross-reactivity of the second binding member with an analog of the analyte, and

means for determining the presence or absence of aggregates.

27. A method for characterizing the binding forces between a first binding member and a second binding member, the method comprising the steps of

(a) providing

(i) a surface that has a first binding member attached thereto and

(ii) a plurality of particles that have a second binding member attached thereto,

(b) contacting the particles with the surface under conditions such that if the first binding member has a binding affinity for the second binding member, a complex is formed and the particle that the second binding member is attached to thereby becomes immobilized with respect to the surface,

(c) applying a force from an ultrasonic power source to the particles, and

(d) monitoring the position of the particles with respect to the surface before, during and/or after step (c).

28. A method for characterizing the binding forces of a plurality of different surface-bound binding members and a particle-bound binding member, the method comprising the steps of

(a) providing

(i) a surface having spatially distinguishable subregions, each subregion having a different surface-bound binding member attached thereto, and

(ii) a plurality of particles that have a particle-bound binding member attached thereto,

(b) contacting the particles with the surface under conditions such that if a surface-bound binding member and a particle-bound binding member have a binding affinity for each other, a complex is formed between the surface-bound binding member and the particle-bound binding member whereby the particles become immobilized with respect to the surface,

(c) directing an ultrasonic force onto the surface wherein the intensity of the ultrasonic force is first initiated at low level that is insufficient to separate the complex and is gradually increased to a higher level that is sufficient to separate the complex

(d) monitoring the position of the particles with respect to the surface before and after step (c).

29. A method for characterizing the binding force of a surface-bound binding member with a plurality of different particle-bound binding members, the method comprising the steps of

(a) providing

(i) a surface that has a surface-bound binding member attached thereto, and

(ii) a plurality of particles of different distinguishable classifications, wherein each classification of particles has a different particle-bound binding member attached thereto,

(b) exposing the surface to the particles under conditions such that if a surface-bound binding member and a particle-bound binding member have a binding affinity for each other, a complex is formed between individual surface-bound binding members and individual particle-

bound binding members whereby the particles become immobilized with respect to the surface,

(c) directing an ultrasonic force onto the surface wherein the intensity of the ultrasonic force is first initiated at low level that is insufficient to separate any complexes that are formed in step (b) and is gradually increased to a higher level that is sufficient to separate the complexes,

(d) monitoring the position of the different classifications of particles with respect to the surface before and after step (c).

30. A method for detecting the presence or amount of an analyte of interest in a test sample, the method comprising the steps of

(a) contacting the test sample with

(i) a surface that has first binding members that bind specifically to the analyte attached thereto, and

(ii) a labeled reagent that includes a second binding member capable of undergoing a selective binding interaction whereby the labeled reagent becomes immobilized specifically with respect to the surface in relation to the amount of the analyte in the test sample,

(b) directing an ultrasonic force onto the surface wherein the intensity of the ultrasonic force is controlled to cause the dislodging any of the labeled reagent that binds non-specifically to the surface or that becomes immobilized on the surface due to cross-reactivity with an analog of the analyte and wherein the intensity of the ultrasonic force is controlled to prevent the dislodging of the labeled reagent that becomes immobilized specifically with respect to the surface in relation to the amount of the analyte in the test sample,

(c) removing any labeled reagent that becomes dislodged as a result of step (b), and

(d) detecting the amount of labeled reagent that remains immobilized with respect to the surface after steps (b) and (c).

31. The method of Claim 30 wherein the intensity of the ultrasonic force is controlled by controlling the amplitude, frequency, duration and/or wave-form of the ultrasonic force.

32. The method of Claim 30 wherein the frequency of the ultrasonic force is between about 80 kHz and about 10 MHz.

33. The method of Claim 30 wherein the ultrasonic force is a pulsed force having a pulse duration of less that about 20 milliseconds.

34. The method of Claim 30 wherein the wave-form of the ultrasonic force is a triangle or saw-tooth.

35. A method for detecting the presence or amount of an analyte of interest in a test sample, the method comprising the steps of

(a) contacting the test sample with

(i) a surface that has first binding members that bind specifically to the analyte attached thereto, and

(ii) a plurality of particles that have second binding members attached thereto, wherein the second binding members are capable of undergoing a selective binding interaction whereby the particles become immobilized specifically with respect to the surface in relation to the amount of the analyte in the test sample,

(b) directing an ultrasonic force onto the surface wherein the intensity of the ultrasonic force is controlled to cause the dislodging any of the analyte or particles that bind non-specifically to the surface or that becomes immobilized on the surface due to cross-reactivity of the second binding members with an analog of the analyte and wherein the intensity of the ultrasonic force is controlled to prevent the dislodging of the particles that become immobilized specifically with respect to the surface in relation to the amount of the analyte in the test sample,

(c) removing any particles that becomes dislodged as a result of step (b), and

(d) monitoring the position of the particles with respect to the surface after steps (b) and (c).

36. A method for detecting the presence or amount of a plurality of different analytes in a test sample, the method comprising the steps of

(a) contacting the test sample with

(i) a surface that spatially distinguishable subregions, wherein each subregion has a different surface-bound binding member attached thereto, wherein each different surface-bound binding member binds specifically to a different analyte, and

(ii) a plurality of sets of particles that have particle-bound binding members attached thereto, wherein the particle-bound binding members are capable of undergoing a selective binding interaction whereby the particles become immobilized specifically with respect to the surface in relation to the amount of an analyte in the test sample, and wherein each set of particles is selective of a different analyte,

(b) directing an ultrasonic force onto the surface wherein the intensity of the ultrasonic force is controlled to cause the dislodging any of the analyte or particles that bind non-specifically to the surface or that becomes immobilized on the surface due to cross-reactivity of the second binding members with an analog of the analyte and wherein the intensity of the ultrasonic force is controlled to prevent the dislodging of the particles that become immobilized specifically with respect to the surface in relation to the amount of the analyte in the test sample,

(c) removing any particles that becomes dislodged as a result of step (b), and

(d) monitoring the position of the particles with respect to the subregions of the surface after steps (b) and (c).

37. A method for detecting the presence of an analyte of interest in a test sample, the method comprising the steps of

(a) contacting the test sample with

(i) a plurality of first particles that have first binding members that bind specifically to the analyte attached thereto, and

(ii) a plurality of second particles that have second binding members attached thereto, wherein the second binding members are capable of undergoing a selective binding interaction whereby second particles, when exposed to first particles that have been exposed to the test sample, bind specifically to the first particles in relation to the amount of the analyte in the test sample and form an aggregate of first particles and second particles,

(b) directing an ultrasonic force to the test sample wherein the intensity of the ultrasonic

force is controlled to cause the dislodging any of the analyte or second particles that bind non-specifically to the first particles or that becomes immobilized on the first particles due to cross-reactivity of the second binding members with an analog of the analyte and wherein the intensity of the ultrasonic force is controlled to prevent the dislodging of the second particles that bind specifically with respect to the first particles in relation to the amount of the analyte in the test sample,

(c) removing any analyte or second particles that becomes dislodged as a result of step (b), and

(d) determining the presence of aggregates of first particles and second particles after steps (b) and (c).